



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-P-1654]

Determination That LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 Milligrams/1 Milliliter, 10 Milliliter Total Fill Volume, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined that LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 milligrams (mg)/1 milliliter (mL), 10 mL total fill volume, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Darren Eicken, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6206, Silver Spring, MD 20993-0002, 240-402-0978.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure.

ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the "listed

drug," which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the "Approved Drug Products with Therapeutic Equivalence Evaluations," which is known generally as the "Orange Book." Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, is the subject of ANDA 40147, held by Hospira, Inc. (Hospira), and was initially approved on June 25, 1997. LEUCOVORIN CALCIUM-PRESERVATIVE FREE is indicated for treatment of megaloblastic anemia and to counteract the therapeutic and toxic effects of folic acid antagonists.

In a letter dated January 14, 2005, Hospira notified FDA that LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, was being

discontinued, and FDA moved the drug product to the "Discontinued Drug Product List" section of the Orange Book.

Gordon Johnston, on behalf of Gordon Johnston Regulatory Consultants, LLC, submitted a citizen petition dated December 13, 2013 (Docket No. FDA-2013-P-1654), under 21 CFR 10.30, requesting that the Agency determine whether LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that this product was not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list LEUCOVORIN CALCIUM-PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, in the "Discontinued Drug Product List" section of the Orange Book. The "Discontinued Drug Product List" delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to LEUCOVORIN CALCIUM-

PRESERVATIVE FREE Injection, 10 mg/1 mL, 10 mL total fill volume, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: June 10, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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